(FILE 'HOME' ENTERED AT 18:02:39 ON 06 NOV 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, CANCERLIT, BIOTECHDS, BIOSIS' ENTERED AT 18:03:15 ON 06 NOV 2002

L1	0	S CAPMTOTHECIN
L2	68	S CAMPTOTHECIN WITH LACTONE
L3	3417957	S ANTISENSE OR OLIGO? OR DNA OR NUCLEIC
L4	23	S L3 AND L2
L5	12	DUP REM L4 (11 DUPLICATES REMOVED)
L6	2350824	S CONJUGATE OR COMPLEX
L7	6	S L6 AND L2
L8	3	DUP REM L7 (3 DUPLICATES REMOVED)
L9	15477	S CAMPTOTHECIN
L10	1669	S L9 AND L6
L11	1355	S L10 AND L3
L12	515	DUP REM L11 (840 DUPLICATES REMOVED)
L13	63	S L12 AND (OLIG? OR ANTISENSE)

L13 ANSWER 40 OF 63 CAPLUS COPYRIGHT 2002 ACS
AN 1997:745976 CAPLUS
DN 128:39530
TI Targeted combination immunotherapy of cancer
IN Griffiths, Gary L.; Hansen, Hans J.
PA Immunomedics, Inc., USA; Griffiths, Gary L.; Hansen, Hans J.
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9741898	A1	19971113	WO 1997-US7395	19970502
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2253904	AA	19971113	CA 1997-2253904	19970502
	AU 9730572	A1	19971126	AU 1997-30572	19970502
	AU 717020	B2	20000316		
	EP 954340	A1	19991110	EP 1997-925434	19970502
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000510119	T2	20000808	JP 1997-540035	19970502
	US 6077499	A	20000620	US 1998-184950	19981103
PRAI	US 1996-17011P	P	19960503		
	WO 1997-US7395	W	19970502		

AB The invention provides a method for effecting therapy of a tumor in a patient, comprising the steps of: (A) administering to the patient a first **conjugate** comprising a targeting moiety, a first member of a binding pair, and a first therapeutic agent, wherein the targeting moiety selectively binds to a marker substance produced by or assocd. with the tumor, and allowing the **conjugate** to localize at the tumor, thereby effecting therapy of the tumor; (B) optionally, administering to the patient a clearing compn., and allowing the clearing compn. to clear non-localized first **conjugate** from circulation; (C) administering to the patient a second **conjugate** comprising a complementary member of the binding pair and a second therapeutic agent, wherein the second therapeutic agent is the same as or different from the first therapeutic agent, and allowing the second **conjugate** to localize at the tumor, thereby effecting therapy of the tumor.

L13 ANSWER 61 OF 63 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
AN 2000-09449 BIOTECHDS
TI New chemotherapeutic compositions comprising an **oligonucleotide -camptothecin** drug **complex**, useful for treating cancers in a combination therapy;
vectors: retro virus, adeno virus, adeno-associated virus, herpes virus, vaccinia virus, liposome-mediated gene transfer
AU Yang D; Demir A S; Chavan A J; Burke T G
PA Univ.Kentucky
LO Lexington, KY, USA.
PI WO 2000021370 20 Apr 2000
AI WO 1998-US20941 14 Oct 1998
PRAI US 1998-20941 14 Oct 1998
DT Patent
LA English
OS WPI: 2000-329047 [28]
AB A chemotherapeutic composition comprising an **oligonucleotide** (O)-**camptothecin** (C) drug **complex** (OC), which incorporates active lactone (C) drug, where the (C) drug dissociates from the (O) within the body, and exerts its therapeutic activities, is claimed. Also claimed is: a method for delivering (O)-stabilized lactone forms of (C) drugs to a host, comprising providing an (OC) as a delivery vehicle, where the (C) drug contains at least one lactone ring, and the (O) is capable of associating with the (C) drug, so that at least some part of the lactone ring is associated with the (O) and protected from hydrolysis, and administering the (OC) to the host. The compositions containing the (OC), which may be incorporated into a viral or non-viral vector are used for combined gene and **camptothecin** drug therapy in the treatment of cancer. The (O) can bind selectively to the lactone forms of (C), conserving the agents in their biologically active lactone forms. The compositions are stabilized over a wide pH range and can provide for the controlled, targeted and stable delivery of (C). (86pp)

L13 ANSWER 3 OF 63 MEDLINE
AN 2002096867 MEDLINE
DN 21671389 PubMed ID: 11724801
TI Design and optimization of camptothecin conjugates of triple helix-forming oligonucleotides for sequence-specific DNA cleavage by topoisomerase I.
AU Arimondo Paola B; Boutorine Alexandre; Baldeyrou Brigitte; Bailly Christian; Kuwahara Masayasu; Hecht Sidney M; Sun Jian-Sheng; Garestier Therese; Helene Claude
CS Laboratoire de Biophysique, UMR 8646 CNRS, Museum National d'Histoire Naturelle, INSERM U201, 43 rue Cuvier, 75231 Paris cedex 05, France.. arimondo@mnhn.fr
NC CA78415 (NCI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Feb 1) 277 (5) 3132-40. Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200202
ED Entered STN: 20020206
Last Updated on STN: 20020301
Entered Medline: 20020228
AB To achieve a sequence-specific DNA cleavage by topoisomerase I, derivatives of the antitumor drug camptothecin have been covalently linked to triple helix-forming oligonucleotides that bind in a sequence-specific manner to the major groove of double-helical DNA. Triplex formation at the target sequence positions the drug selectively at the triplex site, thereby stimulating topoisomerase I-mediated DNA cleavage at this site. In a continuous effort to optimize this strategy, a broad set of conjugates consisting of (i) 16-20-base-long oligonucleotides, (ii) alkyl linkers of variable length, and (iii) camptothecin derivatives substituted on the A or B quinoline ring were designed and synthesized. Analysis of the cleavage sites at nucleotide resolution reveals that the specificity and efficacy of cleavage depends markedly on the length of both the triple-helical structure and the linker between the oligonucleotide and the poison. The optimized hybrid molecules induced strong and highly specific cleavage at a site adjacent to the triplex. Furthermore, the drug-stabilized DNA-topoisomerase I cleavage complexes were shown to be more resistant to salt-induced reversal than the complexes induced by camptothecin alone. Such rationally designed camptothecin conjugates could provide useful antitumor drugs directed selectively against genes bearing the targeted triplex binding site. In addition, they represent a powerful tool to probe

the molecular interactions in the DNA-topoisomerase I complex.

Dh

L5 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

AN 1992:503695 CAPLUS

DN 117:103695

TI The influence of camptothecin on topoisomerase I interaction with genomic sequences

AU Kjeldsen, Eigil; Bendixen, Christian; Thomsen, Bo; Christiansen, Kent; Bonven, Bjarne Juul; Nielsen, Ole Frederick; Westergaard, Ole

CS Dep. Mol. Biol. Plant Physiol., Univ. Aarhus, Aarhus, Den.

SO DNA Topoisomerases Cancer (1991), 148-60. Editor(s): Potmesil, Milan; Kohn, Kurt W. Publisher: Oxford Univ. Press, New York, N. Y. CODEN: 57RWAR

DT Conference

LA English

AB The DNA-topoisomerase I interactions in the presence or absence of camptothecin lactone were studied using enzyme prepns. from human Daudi cells and Tetrahymena thermophila. Topoisomerase I appears to be the primary cellular target for camptothecin antitumor effects.

L5 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS

AN 1997:725563 CAPLUS

DN 128:10127

TI SERS and fluorescence study of the molecular interactions of camptothecins with DNA and DNA topoisomerase I and in their ternary cleavable complexes

AU Chourpa, I.; Riou, J. -F.; Pommier, Y.; Manfait, M.

CS Laboratoire de Spectroscopie Biomoleculaire, IFR 53, UFR de Pharmacie, Reims, 51096, Fr.

SO Spectroscopy of Biological Molecules: Modern Trends, [European Conference on Spectroscopy of Biological Molecules], 7th, Madrid, 1997 (1997), 361-362. Editor(s): Carmona, Pedro; Navarro, Raquel; Hernanz, Antonio. Publisher: Kluwer, Dordrecht, Neth. CODEN: 65FQAE

DT Conference

LA English

AB To study both the qual. and quant. aspects of camptothecin-DNA, camptothecin-topoisomerase I and camptothecin-topoisomerase I-DNA mol. interactions, the authors have applied the spectroscopic approach that combines surface-enhanced Raman scattering (SERS) and fluorescence emission techniques. DNA was modeled using 30-mer synthetic oligonucleotides corresponding to a strong camptothecin-inducible (olg1) or camptothecin-independent cleavage sites (olg2) and a

non-specific oligonucleotide void of GC base pairs (olg3). In previous studies, both SERS and fluorescence emission spectra of camptothecins were very sensitive to the state of the lactone ring. The fluorescence measurements were used to quantify kinetics of the lactone opening in hydrolyzable camptothecins under physiol. conditions. In the present work, the kinetics of the lactone hydrolysis has been studied comparatively for free camptothecins when complexed with one of the oligonucleotides or with topoisomerase I and within their ternary complexes. The ratio-dependent stabilization of the lactone forms of camptothecins in the presence of an excess of olg1 or olg2, but not of olg3. Anal. of the spectral data indicates the low affinity binding of the lactone ring of camptothecins to GC base pairs. These sites coincide with those for topoisomerase I; an addn. of the enzyme to the camptothecin-olg1 and camptothecin-olg2 complexes destabilized the lactone ring of the drug. Moreover, the lactone ring was not stabilized when oligonucleotides were added to the camptothecin-topoisomerase I complexes. Data from the SERS spectroscopy supported these results and allowed more detailed qual. discussion on participation of the lactone and quinoline parts of camptothecins in the mol. interactions of these drugs within the cleavable complexes. The relation of these results with the antitumor activity of camptothecins is discussed.

L5 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
AN 1998:269137 CAPLUS
DN 128:278688
TI DNA Interactions of Two Clinical Camptothecin Drugs Stabilize Their Active Lactone Forms
AU Yang, Danzhou; Strode, J. Thompson; Spielmann, H. Peter; Wang, Andrew H.-J.; Burke, Thomas G.
CS Division of Medicinal Chemistry and Pharmaceutics College of Pharmacy Department of Biochemistry, Markey Cancer Center University of Kentucky, Lexington, KY, 40506, USA
SO Journal of the American Chemical Society (1998), 120(12), 2979-2980 CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The active lactone forms of CPT-11 and topotecan were stabilized through interactions with double stranded DNA; in fact, in the presence of the DNA, the conversion of the inactive carboxylate from to the active lactone form was promoted. The results provide evidence that duplex DNA devoid of topoisomerase I may play a functional role in the biol. activities of the camptothecins through the promotion of active lactone levels within the cell nucleus. The agents may interact directly with DNA prior to the action by topoisomerase I.

oligo-enzyme surface.

L13 ANSWER 42 OF 63 CAPLUS COPYRIGHT 2002 ACS
AN 1997:457111 CAPLUS
DN 127:130544
TI Sequence-Specific Targeting of Duplex DNA Using a Camptothecin-Triple Helix Forming Oligonucleotide Conjugate and Topoisomerase I
AU Matteucci, Mark; Lin, Kuei-Ying; Huang, Teresa; Wagner, Richard; Sternbach, Daniel D.; Mehrotra, Mukund; Besterman, Jeffrey M.
CS Gilead Sciences Inc., Foster City, CA, 94404, USA
SO Journal of the American Chemical Society (1997), 119(29), 6939-6940
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
AB The Topoisomerase I inhibitor, camptothecin, has been conjugated to the 3' end of a triple helix forming oligonucleotide (TFO). This conjugate is shown to be able to recruit the ubiquitous cellular enzyme, Topoisomerase I (Topo I) to a specific site on a targeted duplex DNA. The covalent Topo I-DNA complex results in strand scission upon denaturation. The cleavage occurs in the strand of the duplex which is opposite the polypurine tract recognized by the TFO. The enhancement of sequence-specific targeting of mRNA by the recruitment of cellular enzymes such as RNase H is well known. The camptothecin TFO conjugate is the first demonstration of an ubiquitous cellular enzyme recruitment for the sequence-specific targeting of duplex DNA. Such conjugates are worthy of further study in living cells for the precise targeting of genomic DNA via the recruitment of the cellular enzyme Topo I.

L13 ANSWER 41 OF 63 CAPLUS COPYRIGHT 2002 ACS
AN 1997:725569 CAPLUS
DN 128:10128
TI Conformation and mechanism in DNA-topoisomerase I as a target of antitumor drugs: optical spectroscopy approach
AU Fleury, F.; Ianoul, A.; Kudelina, I.; Bronstein, I.; Alix, A. J. P.; Dodson, G.; Feofanov, A.; Nabiev, I.
CS Laboratoire de Spectroscopie Biomoleculaire, URCA, IFR 53, UFR de Pharmacie, Reims, 51096, Fr.
SO Spectroscopy of Biological Molecules: Modern Trends, [European Conference on Spectroscopy of Biological Molecules], 7th, Madrid, 1997 (1997), 373-374. Editor(s): Carmona, Pedro; Navarro, Raquel; Hernanz, Antonio. Publisher: Kluwer, Dordrecht, Neth.

CODEN: 65FQAE
DT Conference
LA English
AB The authors used steady-state [UV-Resonance Raman (UV-RR)] and kinetic [flow linear dichroism (FLD)] spectroscopic approaches to the study of recombinant human topoisomerase I with supercoiled plasmids and synthetic oligonucleotides (oligos) representing the specific sequences of camptothecin-dependent, camptothecin -independent or suicide DNA cleavage sites. The time dependence of the FLD signal during supercoiled during cleavage by the enzyme was studied. The kinetic consts. of cleavage were detd. and the process of inhibition of the cleavage in the presence of the lactone forms of the drugs (camptothecin, CPT11, SN38 and 10,11-methylenedioxycamptothecin) have been monitored. Kinetics of supercoiled DNA cleavage by the enzyme was found to be different from the Michaelis-Menten law. The relative inhibitory activity of the drugs was detd. from the FLD and correlated with the data of the biochem. assays. Pronounced differences of interactions of camptothecin and its deriv. CPT11 with oligos were found using UV-RR spectroscopy. Some 30-mer oligos were derived from the sequences of the topoisomerase I-induced and camptothecin-enhanced cleavage sites in SV 40 DNA. Camptothecin-enhanced induced well-defined alterations of the oligo structure, whereas CPT11 interacted with oligos weakly and in another manner than camptothecin. Formation of cleavable ternary complexes between CPT11, topoisomerase I and oligos caused CPT11 to interact with oligo in the same fashion as was found for its parent compd., camptothecin, and enhanced this interaction as compared to camptothecin-oligo complexes. The data present evidence of mol. interactions of CPT11 with both other partners (topoisomerase I and oligo) of the ternary cleavable complex at the oligo-enzyme surface.

L13 ANSWER 7 OF 63 MEDLINE
AN 2000015442 MEDLINE
DN 20015442 PubMed ID: 10547719
TI Targeting topoisomerase I cleavage to specific sequences of DNA by triple helix-forming oligonucleotide conjugates. A comparison between a rebeccamycin derivative and camptothecin.
AU Arimondo P B; Bailly C; Boutorine A; Sun J S; Garestier T; Helene C
CS Laboratoire de biophysique, UMR 8646 CNRS-Museum national d'histoire naturelle, Inserm U201, Paris, France.
SO COMPTES RENDUS DE L ACADEMIE DES SCIENCES. SERIE III, SCIENCES DE LA VIE, (1999 Sep) 322 (9) 785-90.

Journal code: 8503078. ISSN: 0764-4469.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
ED Entered STN: 20000204
Last Updated on STN: 20021030
Entered Medline: 20000124
AB Topoisomerase I is an ubiquitous DNA cleaving enzyme and an important therapeutic target in cancer chemotherapy for the camptothecins as well as for indolocarbazole antibiotics such as rebeccamycin and its synthetic derivatives, which stabilize the cleaved DNA -topoisomerase I complex. The covalent linkage of a triple helixforming oligonucleotide to camptothecin or to the indolocarbazole derivative R-6 directs DNA cleavage by topoisomerase I to specific sequences. Sequence-specific recognition of DNA is achieved by the triple helix-forming oligonucleotide, which binds to the major groove of double-helical DNA and positions the drug at a specific site. The efficacy of topoisomerase I-induced DNA cleavage mediated by the rebeccamycin-conjugate and the camptothecin-conjugate was compared and related to the intrinsic potency of the isolated drugs.